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10/525,318	10/07/2005	Natalia N. Bogdanova	38-21(15414)B	5329

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MONSANTO COMPANY
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EXAMINER	
KUBELIK, ANNE R	
ART UNIT	**PAPER NUMBER**
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,318	BOGDANOVA ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,7 and 9-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,7 and 9-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-2, 4, 7 and 9-14 are pending.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-2, 4, 7 and 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Donovan et al (1994, US Patent 5,322,687) in view of Koziel et al (WO 93/07278). The rejection is repeated for the reasons of record as set forth in the Office action mailed 18 May 2009. Applicant's arguments filed 6 November 2009 have been fully considered but they are not persuasive.

The claims are drawn to nucleic acid comprising bases 7-1803 of SEQ ID NO:3, bases 2650-4446 of SEQ ID NO:5, bases 3047-4844 of SEQ ID NO:8, bases 1247-3043 of SEQ ID NO:11 or bases 1658-3454 of SEQ ID NO:13, methods of making plants and plant cells comprising the nucleic acid operably linked to promoters, and plants and plant cells thereby obtained.

Donovan et al (1994, US Patent 5,322,687) teach a nucleic acid encoding amino acids 2-600 of SEQ ID NO:2 and amino acids 3-601 of SEQ ID NOs:4, 7, 10, 12 and 14; the protein they call cryET4 is identical to the instant cry1Bb. Donovan et al also teach a method of producing a transgenic plant resistant to lepidopteran infestation by transformation with the

nucleic acid operably linked to a promoter (column 11, lines 1-12).

Donovan et al also teach nucleic acid encoding a cry protein they call CryET5 and plants comprising both cryET4 and another Cry1Bb protein, cryET5 (column 5, lines 40-42).

Donovan et al do not disclose bases 7-1803 of SEQ ID NO:3, bases 2650-4446 of SEQ ID NO:5, bases 3047-4844 of SEQ ID NO:8, bases 1247-3043 of SEQ ID NO:11 or bases 1658-3454 of SEQ ID NO:13.

Koziel et al teach codon optimization of Cry endotoxin encoding sequences, using codons most preferred in target plants (pg 4, ¶ spanning pg 5-6; pg 15, ¶2, to pg 16, ¶2, examples 2-3, 7). Maize cells that had been transformed with such a sequence had 20,000 X more Cry endotoxin than maize cells that had been transformed with the wild-type sequence (pg 133, ¶2).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to codon optimize the sequence taught by Donovan et al by the method taught by Koziel et al. One of ordinary skill in the art would have been motivated to do so because of the great increase in the level of endotoxin production (Koziel et al, pg 133, ¶2). Bases 7-1803 of SEQ ID NO:3, bases 2650-4446 of SEQ ID NO:5, bases 3047-4844 of SEQ ID NO:8, bases 1247-3043 of SEQ ID NO:11 and bases 1658-3454 of SEQ ID NO:13 are among the possible codon-optimized sequences that encode amino acids 2-600 of SEQ ID NO:2, and amino acids 3-601 of SEQ ID NOs: 7, 10, 12 and 14. Absent a showing that these particular nuclear acids produced unexpected results over what would be expected for other plant codon-optimized sequences that encode these proteins, the claimed sequences are obvious in view of the art. It would be obvious to obtain seed from the transformed plants, as this is the form sold to farmers.

Similarly, SEQ ID NO:3, which encodes the entire cryET4 (cry1Bb) is obvious, as it would have been obvious to one of ordinary skill in the art to codon optimize the sequence taught by Donovan et al by the method taught by Koziel et al. One of ordinary skill in the art would have been motivated to do so because of the great increase in the level of endotoxin production (Koziel et al, pg 133, ¶2).

Applicant urges that Koziel et al teach using other than the most preferred codons at every position only in the context of a combining a partially optimized sequence with an unmodified sequence; the use of "optimized sequences" refers back to a reference to use the most preferred codons for maize; "preferred codon to the most used codon in a specific host cell; thus the only sequence the skilled artisan would be motivated to use would be one that uses the at every position the most preferred codon for the particular host cell; the instant sequences do not have that (response pg 5-6).

This is not found persuasive. Koziel et al's partially optimized sequences means that the skilled artisan would not be motivated to use would be one that uses the at every position the most preferred codon for the particular host cell; Koziel et al particularly includes those in which the only 5% of the codons are optimized (last sentence, second paragraph pg 16). Koziel et al's method is not limited to a particular codon Table. Selection of a different set of sequences upon which to base a codon table would lead one of skill in the art to produce a different sequence than what one would get using the one described in Koziel et al.

Applicant urges that the earlier responses with respect to Donovan et al are incorporated by reference (response pg 6).

This is not found persuasive. The responses made 8 July 2008 were made in response to a rejection under 35 USC 102, not 35 USC 103. The response made 5 April 2009, that the Donovan references had previously been overcome, overlooked the fact that Donovan et al was overcome as reference in a rejection under 35 USC 102, while being applied in a rejection under 35 USC 103. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Donovan et al has never been removed as a reference under 35 USC 103.

4. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Donovan et al in view of Koziel et al as applied to claims 1-2, 4, 7 and 10-14 above, and further in view of Romano et al (WO 2000/11185). The rejection is repeated for the reasons of record as set forth in the Office action mailed 18 May 2009. Applicant's arguments filed 6 November 2009 have been fully considered but they are not persuasive.

The claims are drawn to nucleic acid comprising bases 7-1803 of SEQ ID NO:3, bases 2650-4446 of SEQ ID NO:5, bases 3047-4844 of SEQ ID NO:8, bases 1247-3043 of SEQ ID NO:11 or bases 1658-3454 of SEQ ID NO:13, methods of making plants and plant cells comprising the nucleic acid operably linked to promoters, and plants and plant cells thereby obtained, wherein the sequences are in constructs comprising the P-e35S promoter, the L-Ta.Cab leader sequence, the I-Os.Act1 intron, optionally the TP-Zm.rbcs chloroplast targeting sequence, and the T-Ta.Hsp17 transcription terminator and polyA sequence.

The teachings of Donovan et al in view of Koziel et al are discussed above. Donovan et al in view of Koziel et al do not teach the P-FMV or P-e35S promoters, the L-Ta.Cab leader

sequence, the I-Os.Act1 intron, the TP-Zm.rbcs chloroplast targeting sequence, or the T-Ta.Hsp17 transcription terminator and polyA sequence.

Romano et al teach the P-FMV or P-e35S promoters (pg 22, lines 12-25), the L-Ta.Cab leader sequence (pg 27, lines 3-4), the I-Os.Act1 intron (pg 26, lines 3-5), the TP-Zm.rbcs chloroplast targeting sequence (pg 25, lines 13-22), or the T-Ta.Hsp17 transcription terminator and polyA sequence (pg 51, line 8, to pg 52, line 12), and their use in plant expression vectors (Table 4).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the sequence taught by Donovan et al in view of Koziel et al to use the P-FMV or P-e35S promoters, the L-Ta.Cab leader sequence, the I-Os.Act1 intron, the TP-Zm.rbcs chloroplast targeting sequence, or the T-Ta.Hsp17 transcription terminator and polyA sequence described in Romano et al. One of ordinary skill in the art would have been motivated to do so because Romano et al teach that are they preferred for use in expression of Cry endotoxins ((pg 22, lines 12-25; pg 27, lines 3-4; pg 26, lines 3-5; pg 25, lines 13-22; pg 51, line 8, to pg 52, line 12; Table 4). The resulting expression constructs would be the instant SEQ ID NO:11 and 13.

Applicant urges that the same arguments above apply here (response pg 7).

This is not found persuasive. The response above applies here.

5. Claims 1-2, 4, 7 and 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Donovan et al (1994, US Patent 5,322,687) in view of Brown et al (1997, US Patent 5,689,052).

The claims are drawn to nucleic acid comprising bases 7-1803 of SEQ ID NO:3, bases 2650-4446 of SEQ ID NO:5, bases 3047-4844 of SEQ ID NO:8, bases 1247-3043 of SEQ ID

NO:11 or bases 1658-3454 of SEQ ID NO:13, methods of making plants and plant cells comprising the nucleic acid operably linked to promoters, and plants and plant cells thereby obtained.

The teachings of Donovan et al are discussed above. Donovan et al do not disclose bases 7-1803 of SEQ ID NO:3, bases 2650-4446 of SEQ ID NO:5, bases 3047-4844 of SEQ ID NO:8, bases 1247-3043 of SEQ ID NO:11 or bases 1658-3454 of SEQ ID NO:13.

Brown et al teach a method of modifying a nucleotide sequence for enhance accumulation of the protein in a monocot; in the method rare and semi-rare codons are reduced by substitution of at least some with more preferred monocot codons, using the codon table of Fig 1 as a guide (column 2, line 49, to column 3, line 4; column 5 line 50, to column 6, line 5). They provide an example of the method applied to a Cry endotoxin gene (example 1).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to codon optimize the sequence taught by Donovan et al by the method taught by Brown et al. One of ordinary skill in the art would have been motivated to do so because of the great increase in the level of endotoxin production (Brown et al, column 23, lines 15-45). Bases 7-1803 of SEQ ID NO:3, bases 2650-4446 of SEQ ID NO:5, bases 3047-4844 of SEQ ID NO:8, bases 1247-3043 of SEQ ID NO:11 and bases 1658-3454 of SEQ ID NO:13 are among the possible codon-optimized sequences that encode amino acids 2-600 of SEQ ID NO:2, and amino acids 3-601 of SEQ ID NOs: 7, 10, 12 and 14. Absent a showing that these particular nuclear acids produced unexpected results over what would be expected for other plant codon-optimized sequences that encode these proteins, the claimed sequences are obvious in view of the art. It would be obvious to obtain seed from the transformed plants, as this is the form sold to farmers.

Similarly, SEQ ID NO:3, which encodes the entire cryET4 (cry1Bb) is obvious, as it would have been obvious to one of ordinary skill in the art to codon optimize the sequence taught by Donovan et al by the method taught by Brown et al. One of ordinary skill in the art would have been motivated to do so because of the great increase in the level of endotoxin production (Brown et al, column 23, lines 15-45).

6. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Donovan et al in view of Brown et al as applied to claims 1-2, 4, 7 and 10-14 above, and further in view of Romano et al (WO 2000/11185).

The claims are drawn to nucleic acid comprising bases 7-1803 of SEQ ID NO:3, bases 2650-4446 of SEQ ID NO:5, bases 3047-4844 of SEQ ID NO:8, bases 1247-3043 of SEQ ID NO:11 or bases 1658-3454 of SEQ ID NO:13, methods of making plants and plant cells comprising the nucleic acid operably linked to promoters, and plants and plant cells thereby obtained, wherein the sequences are in constructs comprising the P-e35S promoter, the L-Ta.Cab leader sequence, the I-Os.Act1 intron, optionally the TP-Zm.rbcs chloroplast targeting sequence, and the T-Ta.Hsp17 transcription terminator and polyA sequence.

The teachings of Donovan et al in view of Brown et al are discussed above. Donovan et al in view of Brown et al do not teach the P-FMV or P-e35S promoters, the L-Ta.Cab leader sequence, the I-Os.Act1 intron, the TP-Zm.rbcs chloroplast targeting sequence, or the T-Ta.Hsp17 transcription terminator and polyA sequence.

The teachings of Romano et al are discussed above.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the sequence taught by Donovan et al in view of Brown et al to use the P-

FMV or P-e35S promoters, the L-Ta.Cab leader sequence, the I-Os.Act1 intron, the TP-Zm.rbcs chloroplast targeting sequence, or the T-Ta.Hsp17 transcription terminator and polyA sequence described in Romano et al. One of ordinary skill in the art would have been motivated to do so because Romano et al teach that are they preferred for use in expression of Cry endotoxins ((pg 22, lines 12-25; pg 27, lines 3-4; pg 26, lines 3-5; pg 25, lines 13-22; pg 51, line 8, to pg 52, line 12; Table 4). The resulting expression constructs would be the instant SEQ ID NO:11 and 13.

Conclusion

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, Ph.D., whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

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February 24, 2010

/Anne R. Kubelik/
Primary Examiner, Art Unit 1638